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Evaluating deviations in prostatectomy patients treated with IMRT

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ABSTRACT

Aim: To evaluate the deviations in prostatectomy patients treated with IMRT in order to calculate appropriate margins to create the PTV.
Background: Defining inappropriate margins can lead to underdosing in target volumes and also overdosing in healthy tissues, increasing morbidity.
Material and methods: 223 CBCT images used for alignment with the CT planning scan based on bony anatomy were analyzed in 12 patients treated with IMRT following prostatectomy. Shifts of CBCT images were recorded in three directions to calculate the required margin to create PTV.
Results and discussion: The mean and standard deviation (SD) values in millimetres were -0.05 ± 1.35 in the LR direction, -0.03 ± 0.65 in the SI direction and -0.02 ± 2.05 the AP direction. The systematic error measured in the LR, SI and AP direction were 1.35 mm, 0.65 mm, and 2.05 mm with a random error of 2.07 mm; 1.45 mm and 3.16 mm, resulting in a PTV margin of 4.82 mm; 2.64 mm, and 7.33 mm, respectively.
Conclusion: With IGRT we suggest a margin of 5 mm, 3 mm and 8 mm in the LR, SI and AP direction, respectively, to PTV1 and PTV2. Therefore, this study supports an anisotropic margin expansion to the PTV being the largest expansion in the AP direction and lower in SI.

1. Background

Radiotherapy after prostatectomy aims to reach a higher efficacy of the treatment, by increasing local control and decreasing disease recurrence.[1–4] Recent data reveals that radiotherapy has enhanced survival without disease in patients with T3N0 stage.[3] The development of techniques, like intensity modulated radiotherapy (IMRT), allows the administration of higher doses and more conformational to

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the target volume, sparing healthy tissues.[5–7] However, IMRT does not allow the reduction of treatment margins that are used to account for geometric uncertainties.[8] In this context, image guided radiotherapy (IGRT), associated with IMRT, enables a more exact location of the target volume,[8] allowing the margin reduction.[9]

Geometric uncertainties that arise during the treatment include deviations due to systematic errors and randomized errors.[10] Systematic errors occur during the preparation of the treatment, from the data transference to the treatment administration.[11,12] On the other hand, randomized errors appear during setup and they are due to organ motion.[1] By using imaging protocols it has been possible to reduce systematic errors through online and offline corrections, and randomized errors through online corrections.[5]

The image acquisition to treatment verification results in a dose increment beyond the prescribed dose.[13] However, cone beam computed tomography (CBCT), allows the visualization of treatment target volumes (TTV) and organs at risk (OAR).[14] Thus, corrections are made before the treatment[14] leading to a more precise dose control.[1] Even with image verification, there are still uncertainties associated to treatment.[15] According to the International Commission on Radiation Units and Measurements (ICRU), uncertainties that exist during treatment should imply the definition of margins to create the planning target volume (PTV), which derives from clinic target volume (CTV).[16] With these margins, there is an assurance that CTV receives the prescribed dose,[17] considering setup errors and internal movements of the target.[6]

Today there are consensual guidelines to CTV definition,[18] although there is no evidence of margin dimensions between CTV and PTV.[18,19] According to van Herk et al., when applying the formula $2.5\Sigma + 0.7\sigma$, it is possible to calculate appropriate margin to make sure that 90% of the population receives a 95% minimum of the prescribed dose to the CTV.[15] Defining inappropriate margins can lead to underdosing in target volumes and also an overdosing in healthy tissues, increasing the morbility.[15] Some studies show that surgical bed in patients submitted to prostatectomy presents larger mobility compared with patients that were not subjected to surgery.[20–22] There are imaging strategies, such as portal image, to correct geometric uncertainties that allow the verification of bony anatomy, although this may be insufficient for the correction of uncertainties.[21] On the other hand, CBCT images allow the visualization of soft tissues leading to the improvement in the correction of uncertainties.[21]

2. Aim

The aim of this study is to evaluate the deviations in prostatectomy patients treated with IMRT in order to calculate the appropriate margins to create the PTV.

3. Material and methods

3.1. *Patient characterization*

The present study evaluated 12 prostatectomy patients submitted to radiotherapy at the Hospital of Meixoeiro in Vigo. They were evaluated between March and May 2015. The patient characteristics are described in Table 1.

Table 1 – Patients' characteristics.

Number of patients	12
Age (years)	
Mean	65
Amplitude	54–73
PSA (ng/ml)	
Average	22.56
Amplitude	5.38–48.63
Gleason, *n*	
7	6
8	1
9	5
Total dose (Gy)	
PTV 1	46.39
PTV 2	63.84
Dose per fraction (Gy)	
PTV 1	1.66
PTV 2	2.28
Pathological T stage, *n*	
T2	1
T3	11

3.2. *Computed tomography scan*

All patients performed the bladder and rectum protocol of the institution for the computed tomography (CT). This protocol consists in emptying the rectum with an enema. Regarding the bladder, the patients were instructed to empty it before the simulation/treatment and then intake 1 l of water with 5 ml of Gastrografin®. Patients were positioned in a supine position with their hands on the chest, a pillow under the head and a leg support. Prior to the acquisition of the images, iopremol was administered for the nodes visualization. Image acquisition started in L4 to the lower limit of the smaller trochanter, with slices of 2 mm in the surgical bed and 5 mm in the remaining pelvis.

3.3. *Definition of regions of interest*

The normal tissues including the rectum, bladder, femoral heads and penile bulb were contoured as OAR in Focal® software. The GTV was defined as the surgical bed for all patients. The CTV1 includes the surgical bed and the pelvic lymph nodes. For the PTV1, 8 mm was added to the CTV1 in all directions. The CTV2 was created by adding a margin of 3 mm from GTV. For PTV2 a margin of 6 mm was added to the posterior axis and 8 mm in other directions from the CTV2.

3.4. *Dosimetric planning*

Dosimetric planning was performed in the treatment planning system Xio® 4.80, using IMRT with integrated boost. 9 treatment fields with 6 MV were used in all patients. A total dose of 46.39 Gy was prescribed to the PTV1, with 1.66 Gy/fraction and a total dose of 63.84 Gy was prescribed to PTV2 with 2.28 Gy/fraction (Table 1). All patients were treated in Elekta Synergy™ linear accelerator.

Table 2 – Mean and standard deviation values of the LR, SI and AP.

	LR (mm)	SI (mm)	AP (mm)
Mean ± standard deviation	−0.05 ± 1.35	−0.03 ± 0.65	−0.02 ± 2.05

Abbreviations: LR: left-right; SI: superior-inferior; AP: anterior-posterior.

Table 3 – Systematic and random errors and CTV–PTV margins in the LR, SI and AP direction.

	LR (mm)	SI (mm)	AP (mm)
Systematic errors (Σ)	1.35	0.65	2.05
Random errors (σ)	2.07	1.45	3.16
$2.5\Sigma + 0.7\sigma$	4.82	2.64	7.33

Abbreviations: LR: left-right; SI: superior-inferior; AP: anterior-posterior.

3.5. *Treatment verification*

CBCT images were performed for treatment verification to define corrections to the patient position based on bony anatomy and to evaluate bladder and rectum volumes, compared with CT images. The image protocol is illustrated in Fig. 1.

3.6. *Statistical analysis*

Microsoft Office Excel® 2013 and the Statistical Package for Social Sciences (SPSS) version 22 were used to collect and analyze data and shift the patients.

From this analysis, the mean and the standard deviation of the longitudinal, lateral and vertical deviations were calculated for each patient.

3.7. *Van Herk formula*

The PTV margin was calculated by applying the van Herk Formula,[15] $2.5\Sigma + 0.7\sigma$. The systematic error, $\sum$, is the standard deviation (SD) of mean errors among fractions for each patient and random error is the root mean square of SD observed for each patient.[23]

4. Results

In our study there are 223 CBCT images were acquired from which the shifts were registered and the mean and SD of the left-right (LR), superior-inferior (SI) and anterior-posterior (AP) axis, as presented in Table 2, were calculated.

Table 3 shows the results of the calculated random and systematic errors of the total position error (TPE) and calculated PTV margin. The random errors were superior to systematic errors and we observed that they were higher in the AP direction and lower in the SI direction. Some authors reported the same results as in our study with prostatectomy patients.[24–25]

The higher margin was verified in the AP direction (7.33 mm) and the lower margin in the SI direction (2.64 mm). This can be explained by the direction of the forces exerted

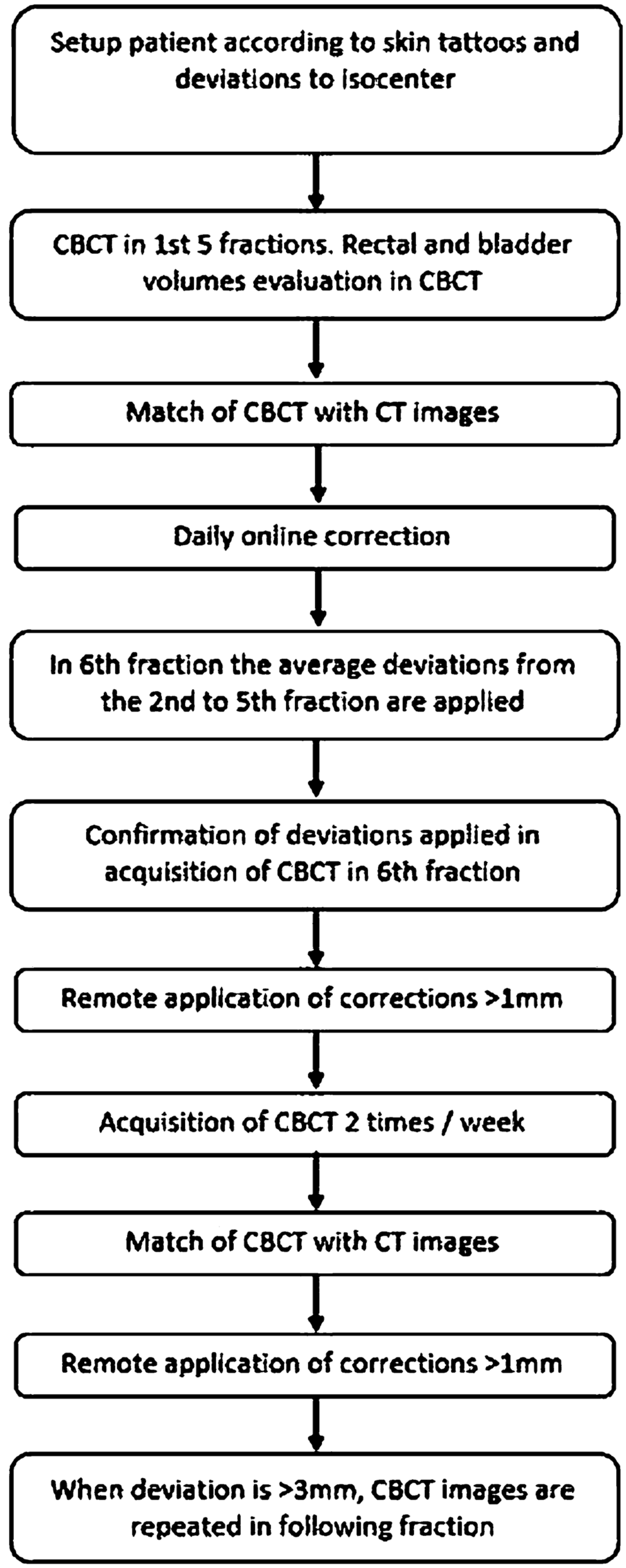

Fig. 1 – Treatment protocol.

Table 4 – Summary of published margin recipes to the TPE based on bony anatomy.

Series (no. of patients)	Comments	Formula	Margin (mm)			Difference (mm)		
			LR	SI	AP	LR	SI	AP
Song et al.[19] ($n = 17$)	2× weekly anterior and lateral kV images	$2.5\sum + 0.7\sigma$	6.0	8.0	9.0	1.2	5.4	1.7
Ålander et al.[24] ($n = 13$)	Daily CBCT	$1.96\sum + 0.7\sigma$	4.9	8.0	7.4	0.1	5.4	0.1
Ost et al.[27] ($n = 15$)	Daily CBCT	$2.5\sum + 0.7\sigma$	8.12	6.04	8.19	3.32	3.44	0.89
Huang et al.[25] ($n = 14$)	Daily CBCT in the 1st 10 fractions	$2.5\sum + 0.7\sigma$	3.87	6.14	6.26	0.93	3.54	1.04

Abbreviations: LR: left-right; SI: superior-inferior; AP: anterior-posterior; CBCT: cone beam computed tomography; $\sum$: SD of systematic errors; σ: root mean square of SD of random errors; TPE: total position error.

Table 5 – Summary of published margin recipes to the PBM based on TPE and PBM.

Series (no. of patients)	Comments	Formula	TPE margin (mm)			PBM margin (mm)		
			LR	SI	AP	LR	SI	AP
Ålander et al.[24] ($n = 13$)	Daily CBCT	$1.96\sum + 0.7\sigma$	4.9	8.0	7.4	1.4	5.9	5.9
Huang et al.[25] ($n = 14$)	Daily CBCT in the 1st 10 fractions	$2.5\sum + 0.7\sigma$	3.87	6.14	6.26	3.14	4.59	4.83
Ost et al.[27] ($n = 15$)	Daily CBCT	$2.5\sum + 0.7\sigma$	8.12	6.04	8.19	7.88	1.78	3.27

Abbreviations: LR: left-right; SI: superior-inferior; AP: anterior-posterior; CBCT: cone beam computed tomography; $\sum$: SD of systematic errors; σ: root mean square of SD of random errors; TPE: total position error; PBM: prostate bed motion.

by the bladder and the rectum during the treatment[26] and by the different location methods yielding different results.[24] The comparison of our results with previous results from the literature is described in Table 4. Hence, we observed that a larger margin is needed in the AP direction for the expansion of PTV in most studies, which is consistent with the results obtained in our study (Table 3).

The highest and lowest recorded values in this axis are presented in the study of Song et al.[19] with 9 mm and Huang et al.[25] with 6.26 mm, respectively.

In general, in the LR direction, the margins required to cover the PTV are smaller. The largest value verified in the LR axis was 8.12 mm in Ost et al.[27] and the smallest value checked was 3.87 mm in Huang et al.[25]. The SI axis, in our study shows a huge difference comparatively to the values presented in Table 4.

The margins achieved with our study resemble mostly those of Ålander et al.[24] in the LR and AP axes showing a difference of 0.1 mm. In comparison to the studies of Ost et al.[27] and Song et al.[19] we found a greater discrepancy in the values LR axes (3.32 mm) and the AP axes (1.7 mm), respectively.

Some authors suggest the implantation of fiducial markers in prostatectomy patients to correct the set-up errors and organ motion.[19,21,24] The placement of surgical clips in surgical bed[19] or gold fiducial seeds allows the identification of prostate bed motion (PBM).[24] Table 5 shows the published margin recipes to the PBM based in fiducial markers position and to the TPE based on bony anatomy.

5. Conclusion

The results of this study confirmed that an 8 mm uniform margin of PTV1 is suitable for the conventional setup in the patient treatment. However, the anisotropic margin of 6 mm in the posterior direction to create PTV2 is inadequate to make sure that 90% of the population receives a minimum of 95% of the prescribed dose to the CTV. In contrast, the 8 mm in the other directions for PTV2 is adequate. Based on our data, we suggest reducing treatment margin in PTV1 and PTV2 to 5 mm and 3 mm in the LR and SI direction, respectively. In the AP direction, we suggest using the same margin in PTV1. In PTV2, we suggest an increase in the posterior direction margin to 8 mm and maintain the same margin for the remaining directions (8 mm). In the future, we propose the implantation of fiducial markers to identify PBM reducing treatment margins with more security and the reduction of toxicity in the surrounding tissues as compared to TPE.

Conflict of interest

None declared.

Financial disclosure

None declared.

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